Artificial skin

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Chapter 6

SUMMARY AND CONCLUSIONS

The skin provides a protective barrier between the living organism and its environment. When the skin is lost or damaged, the individual is threatened by dehydration and infection through the open wound surface.
The aim of this thesis is to analyse the requirements of a skin substitute and to design and test such an "artificial skin" in vitro and in the primary surgical treatment of various skin defects.
Chapter 1 draws up an inventory of the "ideal" artificial skin requirements. In the design of such an artificial skin one is confronted with apparently opposing characteristics: the artificial skin should be "closed" (to prevent bacterial penetration and water evaporation) and at the same time "open" to allow wound drainage and to prevent blister formation.
Chapter 2 outlines the methods and testing models used throughout the study.
Our artificial skin has been designed and constructed as a two layer polyurethane membrane, each with different structures and functions. Its top layer is made microporous. This feature aims to solve the apparent opposing characteristics presented in chapter 1: the micropores are made small ("closed") enough to prevent bacterial penetration and to limit evaporative water loss, but at the same time are made sufficiently "open" to allow effective wound drainage and direct penetration of topical antimicrobial agents.
The artificial skin bottom layer has been designed to adhere immediately and firmly to the wound surface. This was achieved by adding two components to a fibrillar macroporous spongelike structure: micropores and anchoring places for fibrin.
Chapter 3 presents the characteristics of the artificial skin. The features of both top and bottom layer were tested separately. The in vitro tests demonstrated that the microporous top layer prevented bacterial invasion and limited water evaporation but at the same time allowed drainage of fluids and rapid penetration of an antimicrobial agent.
The composite two layer artificial skin was tested in vivo and all previously determined in vitro characteristics of the top layer were confirmed. The bottom layer fixed itself firmly to the wound surface in two sequences: immediate adherence to the wound bed by capillary suction forces from the micropores and secondary adherence by rapid binding of fibrin to its anchoring structures. Moreover, tissue ingrowth in the macroporous bottom layer promoted further adherence. In none of the guinea pig's full thickness skin wounds treated with our artificial skin serous blisters were formed and the artificial skin remained fixed until wound healing was

completed. In contrast the control material Biobrane® fell off from all wounds due to the progressive formation of blisters. This problem of progressive blister formation during the exudative wound healing phase has been described as an enduring problem which occurs under occlusive and semipermeable membranes. Our artificial skin allows satisfactory drainage through the micropores. It should therefore be suitable when treating extensive wounds. Moreover, it turned out that micropores function as selfregulating units: as soon as wound drainage subsides the micropores are closed by the formation of crusty plugs. In this way the artificial skin becomes more occlusive with a limited evaporative water loss similar to living skin. Our artificial skin appeared to have remarkable bactericidal effects: when applied to wounds which were intentionally contaminated with Pseudomonas aeruginosa no infection developed. Therefore it can even be applied to contaminated and infected wounds, without the need for frequent renewal as other skin substitutes demand.

Chapter 4 presents the effect of the two layer artificial skin on wound healing in guinea pigs. A full thickness skin defect heals by contraction of the wound and by the formation of a new epidermis. In man, wound contraction can give unpleasant deformities. In the full thickness guinea pig wounds the artificial skin significantly reduced wound contraction, increased the rate of epithelialization and enhanced the rate of wound healing. In this wound model it was also investigated whether an artificial skin bottom layer should be biodegradable or nondegradable. It appeared that a nondegradable artificial skin is totally shed from the healed wound surface whereas a biodegradable artificial skin leads to the incorporation of the biodegradable polymer particles into the healed "neodermis". As the fate of these polymer particles is unclear, further experiments were carried out with the nondegradable artificial skin.

The rate of wound healing could be enhanced by grafting autologous skin (as mesh or microskin grafts) onto the wound surface. The skin grafts were optimally held in place and the wounds healed faster with less contraction under artificial skin than under conventional paraffin gauze dressings.

Finally, the artificial skin was tested as a wound dressing upon split skin graft donor sites to study its separate effect on the rate of epidermal wound healing, first in the guinea pig and then in man. These studies revealed that split skin graft donor sites treated with artificial skin healed faster than the same wounds treated with conventional paraffin gauzes, which enables earlier reharvesting from the same donor site.

Moreover, the clinical study revealed a few additional properties of the artificial skin: it apeared to be haemostatic and to reduce the formation of serous exudate. All patients reported an absence of pain in the wound half treated with artificial skin, in contrast to the wound half treated with paraffin gauze. Furthermore, almost half of the wounds treated with paraffin gauze became infected whereas none of the adjacent wound halves treated with artificial skin became infected.

This thesis demonstrates that treatment of skin defects with our artificial skin will provide both the patient and his surgeon with a number of substantial benefits above the nowadays available skin substitutes or conventional wound dressings. The artificial skin has many beneficial properties as it:

1. adheres directly and firmly to the wound surface without adhesives and remains permanently in contact with the wound surface until wound healing is complete.
2. is flexible and can be draped smoothly over the wound surface whereby air pockets are removed through the material.
3. reduces pain.
4. is haemostatic.
5. reduces wound exudate formation.
6. allows adequate drainage through the material and prevents the formation of serous blisters under the material. Wound exudate can be absorbed by conventional absorbant dressings which can be replaced after saturation without removal of the artificial skin.
7. prevents bacterial invasion and is suitable for topical antimicrobial treatment.
8. maintains the bactericidal properties of the wound surface and can be applied to contaminated wound surfaces.
9. becomes transparent after application to the wound and allows visual follow up of wound healing.
10. reduces wound contraction.
11. enhances epithelialization and reduces treatment time.
12. does not lead to allergic reactions.
13. is easy to handle and has a long shelf life.
14. can be sterilised by conventional techniques (gas sterilisation and gamma radiation).
15. is cost effective in reducing nurse and physician time due to direct visual wound inspection through the transparent material and the elimination of dressing changes during the healing process.

These established properties of our artificial skin should provide the surgeon with a new tool for the optimal treatment of skin defects.